



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Indinavir (IDV, Crixivan) (Last updated April 27, 2017; last reviewed April 27, 2017)

For additional information see Drugs@FDA: <http://www.accessdata.fda.gov/scripts/cder/daf>

Formulations

Capsules: 100 mg, 200 mg, and 400 mg

Dosing Recommendations

Neonate and Infant Dose:

- Not approved for use in neonates/infants.
- Should not be administered to neonates because of the risks associated with hyperbilirubinemia (kernicterus).

Pediatric Dose:

- Not approved for use in children.
- A range of indinavir doses (234–500 mg/m² body surface area) boosted with low-dose ritonavir has been studied in children (see text below).

Adolescent and Adult Dose:

- 800 mg indinavir plus 100 or 200 mg ritonavir every 12 hours

Selected Adverse Events

- Nephrolithiasis
- Gastrointestinal intolerance, nausea
- Hepatitis
- Indirect hyperbilirubinemia
- Hyperlipidemia
- Hyperglycemia
- Fat maldistribution
- Possible increased bleeding episodes in patients with hemophilia

Special Instructions

- When given in combination with ritonavir, meal restrictions are not necessary.
- Adequate hydration is required to minimize risk of nephrolithiasis (≥48 oz of fluid daily in adult patients).
- If co-administered with didanosine, give indinavir and didanosine ≥1 hour apart on an empty stomach.
- Indinavir capsules are sensitive to moisture; store at room temperature (59–86° F) in original container with desiccant.

Metabolism/Elimination

- Cytochrome P450 3A4 (CYP3A4) inhibitor and substrate
- Dosing in patients with hepatic impairment: Decreased dosage should be used in patients with mild-to-moderate hepatic impairment (recommended dose for adults is 600 mg indinavir every 8 hours). No dosing information is available for children with any degree of hepatic impairment or for adults with severe hepatic impairment.

Drug Interactions (see also the [Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents](#) and <http://www.hiv-druginteractions.org/>)

- *Metabolism:* CYP3A4 is the major enzyme responsible for metabolism. There is potential for multiple drug interactions.
- Avoid other drugs that cause hyperbilirubinemia, such as atazanavir.
- Before administration, a patient's medication profile should be carefully reviewed for potential drug interactions with indinavir.

Major Toxicities

- *More common:* Nephrolithiasis/urolithiasis with indinavir crystal deposit (higher in children (29%) than in adults (12.4%).¹ Nausea, abdominal pain, headache, metallic taste, dizziness, asymptomatic hyperbilirubinemia (10%), lipid abnormalities, pruritus, and rash.
- *Less common (more severe):* Fat maldistribution.
- *Rare:* New-onset diabetes mellitus, hyperglycemia, ketoacidosis, exacerbation of preexisting diabetes mellitus, spontaneous bleeding in hemophiliacs, acute hemolytic anemia, and hepatitis (life-threatening in rare cases).

Resistance

The International Antiviral Society-USA (IAS-USA) maintains a list of updated resistance mutations (see http://iasusa.org/sites/default/files/tam/october_november_2015.pdf#page=10) and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation (see <http://hivdb.stanford.edu/DR/>).

Pediatric Use

Approval

Indinavir has not been approved by the Food and Drug Administration for use in the pediatric population. Although indinavir was one of the first protease inhibitors to be studied in children, its use in pediatrics has never been common and is currently very rare.² **Indinavir is not recommended by Panel members for use in children because of its unfavorable toxicity profile, limited efficacy data, and uncertain pharmacokinetics.**

Efficacy and Pharmacokinetics

Both unboosted and ritonavir-boosted indinavir have been studied in children with HIV infection. An unboosted indinavir dose of 500 to 600 mg/m² body surface area given every 8 hours results in peak blood concentrations and area under the curve slightly higher than those in adults, but considerably lower trough concentrations. A significant proportion of children have trough indinavir concentrations less than the 0.1 mg/L value associated with virologic efficacy in adults.³⁻⁶ Studies in small groups of children of a range of indinavir/ritonavir doses have shown that indinavir 500 mg/m² body surface area plus ritonavir 100 mg/m² body surface area twice daily is probably too high,⁷ that indinavir 234 to 250 mg/m² body surface area plus low-dose ritonavir twice daily is too low,^{8,9} and that indinavir 400 mg/m² body surface area plus ritonavir 100 to 125 mg/m² body surface area twice daily results in exposures approximating those seen with 800 mg indinavir/100 mg ritonavir twice daily in adults, albeit with considerable inter-individual variability and high rates of toxicity.⁹⁻¹¹

References

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